Translation

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

| Applicant's or agent's file reference | FOR FURTHER ACTION | See Form PCT/IPEA/416 |
|---|---|---|
| 11333p | | |
| International application No. | International filing date *(day/month/year)* | Priority date *(day/month/year)* |
| PCT/EP2004/002680 | 15.03.2004 | 02.07.2003 |
| International Patent Classification (IPC) or national classification and IPC | | |
| C12Q1/68 | | |
| Applicant | | |
| LABOR BECKER OLGEMOELLER & KOLLEGEN GBR | | |

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

3. This report is also accompanied by ANNEXES, comprising:

   a. ☒ *(sent to the applicant and to the International Bureau)* a total of 1 sheets, as follows:

      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))

      _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

| | | |
|---|---|---|
| ☒ | Box No. I | Basis of the report |
| ☐ | Box No. II | Priority |
| ☐ | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| ☐ | Box No. IV | Lack of unity of invention |
| ☒ | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| ☐ | Box No. VI | Certain documents cited |
| ☐ | Box No. VII | Certain defects in the international application |
| ☐ | Box No. VIII | Certain observations on the international application |

| Date of submission of the demand | Date of completion of this report |
|---|---|
| Name and mailing address of the IPEA/EP | Authorized officer |
| Facsimile No. | Telephone No. |

**INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY**

International application No.
PCT/EP2004/002680

**Box No. I Basis of the report**

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (Rule 12.3 and 23.1(b))

☐ publication of the international application (Rule 12.4)

☐ international preliminary examination (Rule 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☐ the international application as originally filed/furnished

☒ the description:

pages 1-16 as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☒ the claims:

nos. 6-24 as originally filed/furnished

nos.* _____ as amended (together with any statement) under Article 19

nos.* 1-5 received by this Authority on 16.04.2005 with letter of 16.04.2005

nos.* _____ received by this Authority on _____

☒ the drawings:

sheets 1 as originally filed/furnished

sheets* _____ received by this Authority on _____

sheets* _____ received by this Authority on _____

☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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**Box No. V** **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Claims | 1-24 | YES |
| | Claims | | NO |
| Inventive step (IS) | Claims | | YES |
| | Claims | 1-24 | NO |
| Industrial applicability (IA) | Claims | 1-24 | YES |
| | Claims | | NO |

2. Citations and explanations (Rule 70.7)

1. This report refers to the following search report citation (the reference number will be retained throughout the remainder of the procedure):

D1: US-B1-6 174 670

The present invention relates to a method for qualitative or quantitative detection of a nucleic acid in a sample by amplification of the nucleic acid using a probe.

3. NOVELTY (PCT Article 33(1) and (2))

Document D1 shows (see the abstract) a method for detecting a nucleic acid in a sample by amplification (Real-Time PCR) and hybridisation of the PCR products using a detection probe. However, D1 does not mention carrying out the method with a single-stranded control nucleic acid present in the sample. **Claims 1 to 24 are therefore considered novel**.

4. INVENTIVE STEP (PCT Article 33(3))

Document D1 is considered to be the prior art closest to the subject matter of claim 1.

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

D1 discloses (see example 20, last paragraph; example 21, last paragraph; figure 5, 18-19) a method for qualitative or quantitative detection of a nucleic acid by amplification using one or more probes.

The subject matter of claim 1 differs from what is known from D1 in that the method is carried out with a single-stranded control nucleic acid present in the sample.

The problem addressed by the present invention can thus be seen as that of providing an alternative method for detecting nucleic acids.

The solution proposed in claim 1 involves carrying out the method with a single-stranded control nucleic acid present in the sample.

In the present invention the control nucleic acid is amplified and thus becomes double-stranded. The double-stranded control nucleic acid binds the same probe as the target nucleic acid, but the melting points of the control probe and the target nucleic acid probe and the control nucleic acid probe are different, which means that the two products can be distinguished by analysis. However, double-stranded nucleic acids with these features are mentioned in D1. D1 mentions the use of "competitors", which differ from the target nucleic acid by one nucleic acid (and hence have a different melting temperature). D1 shows that mutated target sequences can be identified comprising PCR amplification products and the probe are different.

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Hence the presence of a single-stranded control nucleic acid in the sample does not result in a surprising technical effect, and therefore claim 1 cannot be considered inventive.

In the light of D1 a person skilled in the art would be aware that the method allows a number of discrepancies in a sequence to be distinguished and quantified, and would therefore be able to design an improved control nucleic acid for distinguishing the target nucleic acids from the control nucleic acid.

Consequently the feature specified in claim 9 ("detection of the nucleic acid at a temperature between 2 and 10°C below the melting temperature of the product of the target nucleic acid and the probe") is just one of a number of obvious possibilities from which a person skilled in the art would choose according to the circumstances in order to solve the problem of interest, without making an inventive contribution. **Claims 9, 10 and 14 to 21** therefore fail to meet the PCT requirements in respect of inventive step.

Claims 12 and 13 relate to a well known method (see, for example, claim 21 in document D1). A combination of this method with that of claim 1 cannot be considered inventive because it does not result in an unexpected effect. **Claims 12 and 13** therefore fail to meet the PCT requirements in respect of inventive step.

In the light of D1, **claims 22 to 24** fail to meet the requirement of PCT Article 33(1), (2) and (3) because the use of known reagents in a known method does not involve

an inventive step.

5. CLOSING REMARKS

5.1 Dependent claims 15, 16 and 19 are unclear because "the sequence range of the control nucleic acid that cannot hybridise either with a detection probe or optionally with a primer" is not defined in the preceding claims (PCT Article 6).

Claims 15 and 19 are also unclear because it is not specified how the sequence range of the control nucleic acid is shortened.

5.2 The term "substantially" in claims 16 and 20 is vague and unclear, and leaves the reader in doubt as to the meaning of the technical feature referred to. The subject matter of the claim is therefore not clearly defined (PCT Article 6).

5.3 The terms "evenly" and "substantially evenly" in claims 21 and 24 are vague and unclear, and leaves the reader in doubt as to the meaning of the technical feature referred to. The subject matter of the claim is therefore not clearly defined (PCT Article 6).

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**Supplemental Box Relating to Sequence Listing**

**Continuation of Box No. I, item 2:**

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:

   a. type of material

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing

   ☒ contained in the international application as filed

   ☐ filed together with the international application in computer readable form

   ☐ furnished subsequently to this Authority for the purposes of search and/or examination

   ☐ received by this Authority as an amendment* on _____

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

* *If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."*